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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,940

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Mitchell Ehren Garber

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Stanford University Office of Technology Licensing

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1643

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,940	Applicant(s) GARBER, MITCHELL EHREN	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 55-57 is/are pending in the application.
- 4a) Of the above claim(s) 55-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-16) in the reply filed on October 3, 2008 is acknowledged. The traversal is on the ground(s) that "...the entire application on the merits, even though the entire application includes claims to independent or distinct inventions", see page 1, 2nd paragraph. This is not found persuasive because within the same section it is noted

"

Examiners must provide reasons and/or examples to support conclusions, but need not cite documents to support the restriction requirement in most cases.

Where plural inventions are capable of being viewed as related in two ways, both applicable criteria for distinctness must be demonstrated to support a restriction requirement.

"

The Examiner actually provided evidence in the Requirement supporting her conclusions, the two groups cited in the Requirement are not so linked as to form a single general concept and the two groups lack the same or corresponding special technical features.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-16 and 55-57 are pending.

Claims 55-57, drawn to non-elected inventions and are not examined on the merits.

Claims 1-16 are examined on the merits.

Specification

7. The attempt to incorporate subject matter into this application by reference to GenBank accession numbers Hs.516830 in claims 3, 8 and 16 is improper because this is essential subject matter. This GenBank number is considered non-patent literature that define the limitations of the claims. This number is subject to change.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-16 are broadly drawn to a method of evaluating a cell's metastatic propensity comprising assaying said cell for the presence of *at least one target protein associated with cellular locomotion*, one listed protein is one of the *cyp4 proteins*. The specification defines target proteins as proteins that may be associated with cellular locomotion and a cellular locomotion protein is defined as a protein that is involved or associated with cellular motility or movement from one location to another, page 11, lines 18-34. Moreover, the CYP4 family consists of 11 subfamilies and one protein from this family has not been defined with any particularity in the specification as to its

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implementation in the claimed method (Gen. Pharmac. 28(3); 351-359, 1997).

Consequently these target proteins associated with cellular locomotion and the genus of cyp4 proteins comprises a number of proteins that have not been adequately defined or characterized. Both genus of proteins may include wild-type proteins, as well as naturally expressed variants. The written description in this instant case has not been adequately defined. There is no SEQ ID number set forth in the claims which corresponds to the listed proteins set forth in claims, which would aid in clearly establishing what Applicants are in possession. The written description is not commensurate in scope with the claims that embody the terms, such as tripartite-containing motif 29 (TRIM29).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*. (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the nucleic acid and the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is

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part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed it is not clear what Applicants have possession in regard to the broad terms, target protein associated with cellular locomotion and cyp4 proteins. This claim language encompasses variants and mutants and polypeptides that share less than 100% sequence identity with the proteins. The specification does not evidence the possession of all the possible mutant polypeptides. There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims do not meet the written description provision of 35 U.S.C. 112, first paragraph.

5. Claims 3, 9 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Moreover, the specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper.

An application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See *In re Fouche*, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Reasonable correlation must exist between the scope of the claims and scope of

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enablement set forth. Without sufficient guidance, the implementation of the claimed method utilizing sequences based on changeable accession numbers, which possibly represent different sequences, would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "leading edge" in claims 4 and 5 are indefinite in that the term is superfluous and does not further clarify the claimed subject matter. Accordingly, the metes and bounds cannot be determined.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 2, 4-7 and 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001). Ricci discloses a method of assaying for the presence of neurotrophic tyrosine kinase receptor type 2 (NTRK2/TrkB), as well as other proteins associated with cellular locomotion in membranes from human bronchioloalveolar carcinoma, adenocarcinoma, squamous cell carcinoma and small cell lung cancer (SCLC) using cytoplasmic immunostaining, see Figure 2 on page 441; and page 444, bridging paragraph of columns 1 and 2, Table 2.

10. Claims 1-4, 6-11 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Application Publication number US 2002/0142981 A1 (publication date October 3, 2002). The publication discloses assaying markers for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084. The nucleus-associated ribbon-like structure proteins, leukotriene B4 12-hydroxydehydrogenase (LTB4DH) and a cyp4 protein, cytochrome P450 were assayed, see page 41, Table 6B.

11. Claims 1-4 and 6-16 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003). The publication discloses methods of classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, such as cellular locomotion proteins,

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tripartite-containing motif 29 (TRIM29) and pregnancy-induced growth inhibitor (OKL38), see abstract; page 24 beginning with Example 13; page 29; and page 34.

12. Claims 1-4 and 6-16 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003). The publication discloses methods for characterizing and diagnosing lung cancer comprising assaying solid tumor cancer markers in samples of tissue from subjects, see abstract; page 5, section 0050; page 6, sections 0065-0067; and page 11, section 0113. The lung cancer types are small-cell lung, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung, see page 5, section 0050. The following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001), and further in view of U.S. Patent Application Publication number US 2002/0142981 A1 (publication date October

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3, 2002), U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003) and U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003). The teachings of Ricci have been presented in the first cited 102(b) rejection. Ricci does not teach assaying nucleus-associated ribbon-like structure proteins, LTB4DH and a cyp4 protein, cytochrome P450.

However, the publication '2981 teaches assaying markers, LTB4DH and cytochrome P450 for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084; and see page 41, Table 6B. Publication '3391 teaches methods classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, as well cellular locomotion proteins, TRIM29, OKL38, see abstract; page 24 beginning with Example 13; page 29; and page 34. Publication '19256 teaches The following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include additional candidate biomarkers in a method of diagnosing a neoplastic disease. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary references teach these markers' expression is consistent with solid cancer cell growth, see page 1, sections 0008 and 0009 of publication '2981.

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15. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication number US 2002/0142981 A1 (publication date October 3, 2002), and further in view of Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001), and further in view of U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003) and U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003).

Conclusion

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

-Troyanskaya et al. Nonparametric methods for identifying differentially expressed genes in microarray data. *Bionformatics* 18(11): 1454-1461, 2002.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached on 7:30 am to 6:30 pm, Monday through Saturday with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
10 November 2008
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643